Title Synthesis of Oligonucleotide Arrays...

Inventors: Glenn H. McGall



Figure 1A

 $P_X$  = phosphoramidite, H-phosphonate or phosphate

Y = one of the general structures in Figures 1B-1I ( $R_1$  = -H, alkyl or aryl):

Figure 1B

 $o\text{-}nitrobenzyl thio ethyloxy carbonyl\ (NBTEOC)$ 

Figure 1C

o-nitrophenylaminocarbonyl (NPAC)

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o-nitrophenoxycarbonyl (N2POC)

Figure 1E

m-nitrophenoxycarbonyl (N3POC)

Figure 1F

o-nitrophenylthioethyloxycarbonyl



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#### Figure 1G

α-methyl-8-nitronaphthylmethoxycarbonyl (MeNMOC)

#### Figure 1H

6-substituted 2-(o-nitrophenyl)-2-propyloxycarbonyl (6NPPOC)

A = O, S, N-alkyl, N-aryl,  $(CH_2)_n$ , where n = 0 to about 3 B = aprotic weakly basic group (e.g., N-alkylimidazole)

### Figure 1I

cyclic o-nitrobenzyloxycarbonyl

A = O, S, N-alkyl, N-aryl,  $(CH_2)_n$ , where n = 0 to about 3 B = aprotic weakly basic group (e.g., N-alkylimidazole)



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Figure 2A

TEMPOC

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#### Figure 2B Coupling Efficiency Data

Y	Stepwise yield	photolysis conditions
(MeNPOC-control)	about 88 %	nonpolar solvent
NO <sub>2</sub> CH <sub>3</sub>	about 85 %	МеОН
NO <sub>2</sub>	95 %	DMSO
Me NO2	94 %	Nucleophilic solvent (MeOH)
NO <sub>2</sub>	about 80 %	Nucleophilic solvent (MeOH)
MeO O O O O O O O O O O O O O O O O O O	about 75 %	Nucleophilic solvent (MeOH)
NO <sub>2</sub> CH <sub>3</sub>	90 %	basic solvent (1 % NMI/DMSO)
Me O O O O O	96 %	DMSO

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# Figure 3

# 5'-TEMPOC-T-Phosphoramidite

- 1. Dyer, et al. JOC 64: 7988 (1999) 2. Tetrahedron Lett., 38(52), 8933-4 (1997) 3. McGall, et al. JACS 119: 5081 (1997)

- 4. Triphosgene may work equally well for this step.
  5. Chloroformate can probably be used without purification.

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### Figure 4

### Synthesis of NINOC-T-CEP

R = Me, MeO

R = H, alkyl, alkoxy

- 1. Bronridge, et al. (1998) J. Med. Chem. 41: 1598.
- 2. (i) Brooker, L.S., et al. (1953) US Pat. 2,646,430; (ii) Boekelheide, et at. (1954) J. Org. Chem. 19: 504.; (iii) Bennet, et al (1941) J. Chem Soc. 74: 244.
- 3. Mortensen, et al. (1996) Org. Prep. Proc. Int. 28: 123.

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Figure 5

### Me2NPOC-T-CEP

MeO NO<sub>2</sub> 
$$\frac{(COCl_2)_2 / THF}{MeO}$$
 NO<sub>2</sub>

$$\frac{(iPr_2N)_2POCE}{(iPr_2N)_2NH/}$$
tetrazole

NC

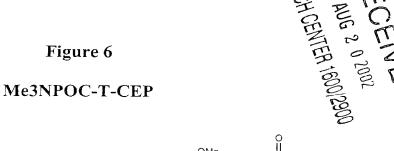
NO

NiPr<sub>2</sub>

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Synthesis of Oligonucleotide Arrays

Inventors: Glenn H. McGall



(ALH 32,927-4)

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# Figure 7

# NP2POC-T-CEP

$$\frac{(iPr_2N)_2POCE}{(iPr_2N)_2NH/}$$
tetrazole

NC

NO2

NO2

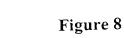
NiPr<sub>2</sub>

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# NNEOC-T-CEP

$$\begin{array}{c|c} & & & \\ &$$